

Exhibit B.pdf

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<!--StartFragment-->RESULT 2
MCTS1_HUMAN
ID      MCTS1_HUMAN              Reviewed;              181 AA.
AC      Q9ULC4; Q502X6;
DT      22-JUL-2008, integrated into UniProtKB/Swiss-Prot.
DT      01-MAY-2000, sequence version 1.
DT      16-DEC-2008, entry version 58.
DE      RecName: Full=Malignant T cell amplified sequence 1;
DE      Short=MCT-1;
DE      AltName: Full=Multiple copies T-cell malignancies;
GN      Name=MCTS1; Synonyms=MCT1;
OS      Homo sapiens (Human).
OC      Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC      Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;
OC      Catarrhini; Hominidae; Homo.
OX      NCBI_TaxID=9606;
RN      [1]
RP      NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM 1), FUNCTION, AND TISSUE
RP      SPECIFICITY.
RX      MEDLINE=98438033; PubMed=9766643;
RA      Prosniak M., Dierov J., Okami K., Tilton B., Jameson B., Sawaya B.E.,
RA      Gartenhaus R.B.;
RT      "A novel candidate oncogene, MCT-1, is involved in cell cycle
RT      progression.";
RL      Cancer Res. 58:4233-4237(1998).
RN      [2]
RP      NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM 1).
RX      PubMed=16533400; DOI=10.1186/1471-2164-7-48;
RA      Kemmer D., Podowski R.M., Arenillas D., Lim J., Hodges E., Roth P.,
RA      Sonhammer E.L.L., Hoeoeg C., Wasserman W.W.;
RT      "NovelPam3000 -- uncharacterized human protein domains conserved
RT      across model organisms.";
RL      BMC Genomics 7:48-48(2006).
RN      [3]
RP      NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA] (ISOFORM 1).
RX      PubMed=14702039; DOI=10.1038/ng1285;
RA      Ota T., Suzuki Y., Nishikawa T., Otsuki T., Sugiyama T., Irie R.,
RA      Wakamatsu A., Hayashi K., Sato H., Nagai K., Kimura K., Makita H.,
RA      Sekine M., Obayashi M., Nishi T., Shibahara T., Tanaka T., Ishii S.,
RA      Yamamoto J., Saito K., Kawai Y., Isono Y., Nakamura Y., Nagahari K.,
RA      Murakami K., Yasuda T., Iwayanagi T., Wagatsuma M., Shiratori A.,
RA      Sudo H., Hosoiri T., Kaku Y., Kodaira H., Kondo H., Sugawara M.,
RA      Takahashi M., Kanda K., Yokoi T., Furuya T., Kikkawa E., Omura Y.,
RA      Abe K., Kamihara K., Katsuta N., Sato K., Tanikawa M., Yamazaki M.,
RA      Minomiya K., Ishibashi T., Yamashita H., Murakawa K., Fujimori K.,
RA      Tanai H., Kimata M., Watanabe M., Hiraoka S., Chiba Y., Ishida S.,
RA      Ono Y., Takiguchi S., Watanabe S., Yosida M., Hotuta T., Kusano J.,
RA      Kanehori K., Takahashi-Fujii A., Hara H., Tanase T.-O., Nomura Y.,
RA      Togiya S., Komai F., Hara R., Takeuchi K., Arita M., Imose N.,
RA      Musashino K., Yuuki H., Oshima A., Sasaki N., Aotsuka S.,
RA      Yoshikawa Y., Matsunawa H., Ichihara T., Shiohara N., Sano S.,
RA      Moriya S., Momiyama H., Satoh N., Takami S., Terashima Y., Suzuki O.,
RA      Nakagawa S., Senoh A., Mizoguchi H., Goto Y., Shimizu F., Wakebe H.,
RA      Hishigaki H., Watanabe T., Sugiyama A., Takemoto M., Kawakami B.,
RA      Yamazaki M., Watanabe K., Kumagai A., Itakura S., Fukuzumi Y.,
RA      Fujimori Y., Komiyama M., Tashiro H., Tanigami A., Fujiwara T.,
RA      Ono T., Yamada K., Fujii Y., Ozaki K., Hirao M., Ohmori Y.,
RA      Kawabata A., Hikiji T., Kobatake N., Inagaki H., Ikema Y., Okamoto S.,
RA      Okitani R., Kawakami T., Noguchi S., Itoh T., Shigeta K., Senba T.,
RA      Matsumura K., Nakajima Y., Mizuno T., Morinaga M., Sasaki M.,
RA      Togashi T., Oyama M., Hata H., Watanabe M., Komatsu T.,

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RA Mizushima-Sugano J., Satoh T., Shirai Y., Takahashi Y., Nakagawa K.,
 RA Okumura K., Nagase T., Nomura N., Kikuchi H., Masuho Y., Yamashita R.,
 RA Nakai K., Yada T., Nakamura Y., Ohara O., Isogai T., Sugano S.;
 RT "Complete sequencing and characterization of 21,243 full-length human
 RT cDNAs.";
 RL Nat. Genet. 36:40-45(2004).
 RN [4]
 RP NUCLEOTIDE SEQUENCE [LARGE SCALE GENOMIC DNA].
 RA Mural R.J., Istrail S., Sutton G.G., Florea L., Halpern A.L.,
 RA Mobarry C.M., Lippert R., Walenz B., Shatkay H., Dew I., Miller J.R.,
 RA Flanigan M.J., Edwards N.J., Bolanos R., Fasulo D., Halldorsson B.V.,
 RA Hannerhalli S., Turner R., Yooseph S., Lu F., Nusskern D.R.,
 RA Shue B.C., Zheng X.H., Zhong F., Delcher A.L., Huson D.H.,
 RA Kravitz S.A., Mouchard L., Reinert K., Remington K.A., Clark A.G.,
 RA Waterman M.S., Eichler E.E., Adams M.D., Hunkapiller M.W., Myers E.W.,
 RA Venter J.C.;
 RL Submitted (SEP-2005) to the EMBL/GenBank/DBJ databases.
 RN [5]
 RP NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA] (ISOFORMS 1 AND 2).
 RC TISSUE=Chondrosarcoma, and Eye;
 RX PubMed=15489334; DOI=10.1101/gr.2596504;
 RG The MGC Project Team;
 RT "The status, quality, and expansion of the NIH full-length cDNA
 RT project: the Mammalian Gene Collection (MGC).";
 RL Genome Res. 14:2121-2127(2004).
 RN [6]
 RP FUNCTION.
 RX PubMed=10440924;
 RX DOI=10.1002/(SICI)1097-4644(19990915)74:4<544::AID-JCB4>3.3.CO;2-W;
 RA Dierov J., Prosniak M., Gallia G., Gartenhaus R.B.;
 RT "Increased G1 cyclin/cdk activity in cells overexpressing the
 RT candidate oncogene, MCT-1.";
 RL J. Cell. Biochem. 74:544-550(1999).
 RN [7]
 RP FUNCTION, SUBCELLULAR LOCATION, AND INDUCTION.
 RX PubMed=11709712; DOI=10.1038/sj.onc.1204881;
 RA Herbert G.B., Shi B., Gartenhaus R.B.;
 RT "Expression and stabilization of the MCT-1 protein by DNA damaging
 RT agents.";
 RL Oncogene 20:6777-6783(2001).
 RN [8]
 RP FUNCTION.
 RX PubMed=12637315; DOI=10.1182/blood-2002-11-3486;
 RA Shi B., Hsu H.-L., Evens A.M., Gordon L.I., Gartenhaus R.B.;
 RT "Expression of the candidate MCT-1 oncogene in B- and T-cell lymphoid
 RT malignancies.";
 RL Blood 102:297-302(2003).
 RN [9]
 RP FUNCTION.
 RX PubMed=16322206; DOI=10.1158/0008-5472.CAN-05-0845;
 RA Levenson A.S., Thurn K.E., Simons L.A., Veliceasa D., Jarrett J.,
 RA Osipo C., Jordan V.C., Volpert O.V., Satcher R.L. Jr.,
 RA Gartenhaus R.B.;
 RT "MCT-1 oncogene contributes to increased in vivo tumorigenicity of
 RT MCF7 cells by promotion of angiogenesis and inhibition of apoptosis.";
 RL Cancer Res. 65:10651-10656(2005).
 RN [10]
 RP FUNCTION.
 RX PubMed=15897892; DOI=10.1038/sj.onc.1208680;
 RA Hsu H.-L., Shi B., Gartenhaus R.B.;
 RT "The MCT-1 oncogene product impairs cell cycle checkpoint control and

RT transforms human mammary epithelial cells.";
 RL Oncogene 24:4956-4964(2005).
 RN [11]
 RP FUNCTION, SUBCELLULAR LOCATION, PUA DOMAIN, AND INTERACTION WITH DENR.
 RX PubMed=16982740; DOI=10.1158/0008-5472.CAN-06-1999;
 RA Reinert L.S., Shi B., Nandi S., Mazan-Mamczarz K., Vitolo M.,
 RA Bachman K.E., He H., Gartenhaus R.B.;
 RT "MCT-1 protein interacts with the cap complex and modulates messenger
 RT RNA translational profiles.";
 RL Cancer Res. 66:8994-9001(2006).
 RN [12]
 RP FUNCTION.
 RX PubMed=17416211; DOI=10.1016/j.dnarep.2007.02.028;
 RA Hsu H.-L., Choy C.O., Kasiappan R., Shih H.-J., Sawyer J.R.,
 RA Shu C.-L., Chu K.-L., Chen Y.-R., Hsu H.-F., Gartenhaus R.B.;
 RT "MCT-1 oncogene downregulates p53 and destabilizes genome structure in
 RT the response to DNA double-strand damage.";
 RL DNA Repair 6:1319-1332(2007).
 RN [13]
 RP FUNCTION, PHOSPHORYLATION, AND MUTAGENESIS OF THR-81 AND SER-118.
 RX PubMed=17016429; DOI=10.1038/sj.onc.1210030;
 RA Nandi S., Reinert L.S., Hachem A., Mazan-Mamczarz K., Hagner P.,
 RA He H., Gartenhaus R.B.;
 RT "Phosphorylation of MCT-1 by p44/42 MAPK is required for its
 RT stabilization in response to DNA damage.";
 RL Oncogene 26:2283-2289(2007).
 CC -!- FUNCTION: Anti-oncogene that play a role in cell cycle regulation;
 CC decreases cell doubling time and anchorage-dependent growth;
 CC shortens the duration of G1 transit time and G1/S transition. When
 CC constitutively expressed, increases CDK4 and CDK6 kinases activity
 CC and CCND1/cyclin D1 protein level, as well as G1 cyclin/CDK
 CC complex formation. Plays a role as translation enhancer; Recruits
 CC the density-regulated protein/DENR and binds to the cap complex of
 CC the 5'-terminus of mRNAs, subsequently altering the mRNA
 CC translation profile; Up-regulates protein levels of BCL2L2, TFDPL1,
 CC MRE11A, CCND1 and E2F1, while mRNA levels remains constant.
 CC Hyperactivates DNA damage signaling pathway; increased gamma-
 CC irradiation-induced phosphorylation of histone H2AX, and induces
 CC damage foci formation. Increases the overall number of chromosomal
 CC abnormalities such as larger chromosomes formation and multiples
 CC chromosomal fusions when over-expressed in gamma-irradiated cells.
 CC May play a role in promoting lymphoid tumor development: lymphoid
 CC cell lines over-expressing MCT1 exhibit increased growth rates
 CC and display increased protection against apoptosis. May contribute
 CC to the pathogenesis and progression of breast cancer via promotion
 CC of angiogenesis through the decline of inhibitory
 CC THBS1/thrombospondin-1, and inhibition of apoptosis. Involved in
 CC the process of proteasome degradation to down-regulate Tumor
 CC suppressor p53/TP53 in breast cancer cell; Positively regulates
 CC phosphorylation of MAPK1 and MAPK3.
 CC -!- SUBUNIT: Interacts (via PUA domain) with DENR.
 CC -!- SUBCELLULAR LOCATION: Cytoplasm. Note=Nuclear relocalization after
 CC DNA damage.
 CC -!- ALTERNATIVE PRODUCTS:
 CC Event=Alternative splicing; Named isoforms=2;
 CC Name=1;
 CC IsoId=Q9ULC4-1; Sequence=Displayed;
 CC Name=2;
 CC IsoId=Q9ULC4-2; Sequence=VSP_034856;
 CC -!- TISSUE SPECIFICITY: Ubiquitous. Over-expressed in T-cell lymphoid
 CC cell lines and in non-Hodgkin lymphoma cell lines as well as in a

CC subset of primary large B-cell lymphomas.
 CC -!- INDUCTION: By DNA damaging agents such as gamma irradiation,
 CC adriamycin or taxol in lymphoid cells, but not by stress stimuli
 CC such as heat shock. This induction of protein expression does not
 CC occur at the RNA level, and does not require new protein
 CC synthesis.
 CC -!- DOMAIN: The PUA RNA-binding domain is critical for cap binding,
 CC but not sufficient for translation enhancer function. MCT1 N-
 CC terminal region is required to enhance translation possibly through
 CC interaction with other proteins.
 CC -!- PTM: Phosphorylation is critical for stabilization and promotion
 CC of cell proliferation.
 CC -!- SIMILARITY: Belongs to the MCT1 family.
 CC -!- SIMILARITY: Contains 1 PUA domain.
 CC -----
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 CC -----
 DR EMBL; AB034206; BAA86055.1; -; mRNA.

Query Match 100.0%; Score 181; DB 1; Length 181;
 Best Local Similarity 100.0%; Pred. No. 3.6e-184;
 Matches 181; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 MFKKFDEKENVSNICQLKTSVIRGIKNQLIEQFPGIEPWLNQIMPKKDPVKIVRCHEHIE 60
Db      1 MFKKFDEKENVSNICQLKTSVIRGIKNQLIEQFPGIEPWLNQIMPKKDPVKIVRCHEHIE 60

Qy      61 ILTVNGELLFFRQREGPFYPTLRLLHKYFFILPHQQVDKGAIKFVLSGANIMCPGLTSPG 120
Db      61 ILTVNGELLFFRQREGPFYPTLRLLHKYFFILPHQQVDKGAIKFVLSGANIMCPGLTSPG 120

Qy      121 AKLYPAAVDITIVAIMAEGKQHALCVGVMMKMSAEDIEKVNGKIGIENIHLYNDGLWHMKT 180
Db      121 AKLYPAAVDITIVAIMAEGKQHALCVGVMMKMSAEDIEKVNGKIGIENIHLYNDGLWHMKT 180

Qy      181 K 181
Db      181 K 181
<!--EndFragment-->

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